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=> D HIS

     (FILE 'HOME' ENTERED AT 17:38:04 ON 07 JUL 2003)

     FILE 'MEDLINE' ENTERED AT 17:38:13 ON 07 JUL 2003
L1             3 S THREONINE(3A)274
L2             1 S VALINE(3A)274
L3             0 S L1 AND L2
L4             4 S L1 OR L2

     FILE 'MEDLINE, SCISEARCH, EMBASE, CAPLUS, BIOSIS, LIFESCI, CONFSCI'
     ENTERED AT 17:42:15 ON 07 JUL 2003
L5            19 S L1
L6            19 S THREONINE(3A)274
L7            11 S VALINE(3A)274
L8             1 S L1 AND L2
L9            29 S L1 OR L2
L10            0 S L9 NOT L4

     FILE 'WPIDS' ENTERED AT 17:45:45 ON 07 JUL 2003
L11            1 S L5
L12            1 S L6
L13            0 S L7

     FILE 'USPATFULL' ENTERED AT 17:47:05 ON 07 JUL 2003
L14           83 S L6
L15           10 S L7
L16            2 S L1 AND L2
L17           91 S L1 OR L2

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L8 ANSWER 1 OF 1 SCISEARCH COPYRIGHT 2003 THOMSON ISI
AN 2003:452849 SCISEARCH
GA The Genuine Article (R) Number: 658QZ
TI Functional expression of a **valine-274** to **threonine** mutation (V274T) in rat alpha 7 nicotinic acetylcholine receptors (nAChR) in recombinant GH4C1 cells
AU David J (Reprint); Misner D; Martin R; Nguyen D; Lansing C; Madden F; Dietrich P; Vivian J; Bonhaus D
CS Roche Biosci, CNS Neurobiol Unit, Palo Alto, CA 94304 USA
CYA USA
SO FASEB JOURNAL, (14 MAR 2003) Vol. 17, No. 4, Part 1, Supp. [S], pp. A627-A627.
Publisher: FEDERATION AMER SOC EXP BIOL, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814-3998 USA.
ISSN: 0892-6638.
DT Conference; Journal
LA English
REC Reference Count: 0

L4 ANSWER 1 OF 4 MEDLINE
AN 1999180249 MEDLINE
DN 99180249 PubMed ID: 10082212
TI Gain of function mutation of the alpha7 nicotinic receptor: distinct pharmacology of the human alpha7V274T variant.
AU Briggs C A; McKenna D G; Monteggia L M; Touma E; Roch J M; Arneric S P; Gopalakrishnan M; Sullivan J P
CS Neuroscience Research, Abbott Laboratories, Abbott Park, IL 60064, USA.. clark.briggs@abbott.com
SO EUROPEAN JOURNAL OF PHARMACOLOGY, (1999 Feb 5) 366 (2-3) 301-8. Journal code: 1254354. ISSN: 0014-2999.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199904
ED Entered STN: 19990511
Last Updated on STN: 19990511
Entered Medline: 19990427
AB In the human alpha7 nicotinic receptor, **valine-274** in the pore-lining transmembrane-2 region was mutated to threonine to produce the variant human alpha7V274T, which was evaluated electrophysiologically following expression in Xenopus laevis oocytes. Inward current rectification was strong in human alpha7V274T as in the human alpha7 wild type nicotinic receptor. However, human alpha7V274T was 100-fold more sensitive to the nicotinic receptor agonists acetylcholine, (-)-nicotine and 1,1-dimethyl-4-phenylpiperazinium. Choline also activated human alpha7V274T (EC50 = 12 microM) and was 82-fold more potent than at human alpha7 wild type nicotinic receptor. (-)-Cotinine, (2,4)-dimethoxybenzylidene anabaseine (GTS-21) and 2-methyl-3-(2-(S)-pyrrolidinylmethoxy)pyridine (ABT-089), weak partial agonists at human alpha7 wild type, were much stronger agonists at human alpha7V274T with EC50 values of 70 microM, 4 microM and 28 microM and fractional activation values of 93%, 96% and 40%, respectively. However, (-)-lobeline, a human alpha7 wild type nicotinic receptor antagonist, and dihydro-beta-erythroidine, which activates chick mutagenized alpha7 nicotinic receptors, had only weak agonist-like activity at human alpha7V274T (< or = 4% of the maximal acetylcholine response). Methyllycaconitine, mecamylamine, d-tubocurarine and dihydro-beta-erythroidine retained antagonist activity and, indeed, appeared to be at least as potent at human alpha7V274T as at human alpha7 wild type. These results support and extend the concept that human nicotinic receptor pharmacology can be profoundly altered by single amino acid changes in the pore-lining segment.